Remarks

Claims 36-56 are pending. Claim 55 has been cancelled. Claims 40-49 and 56 have been amended. A copy of the claims marked up as amended is attached.

Election/Restrictions

The Examiner considered claim 55 to be independent or distinct from the other pending claims and treated the latter as having been constructively elected. Applicants hereby cancel claim 55 but reserve the rights to pursue the same in the future in a divisional application.

Claim Rejection Under 35 U.S.C. §112 ¶2

Claims 40-45 and 47-49 have been rejected under 35 U.S.C. §112 ¶2 as being indefinite. The Examiner suggested that the recitation of "per ml" was unclear. Applicants have amended claims 40-45, 47, and 48 to recite "per ml of the composition" to clarify any potential confusion. The Examiner also suggested that the concentration level in plasma as recited in claim 49 was vague as to whether it was before or after administration. Applicants have amended claim 49 to specifically recite "post-administration."

Accordingly, withdrawal of this rejection is requested.

Claim Rejection Under 35 U.S.C. §102

Claim 46 has been rejected under 35 U.S.C. §102 as being anticipated by Valavichyus *et al.* The Examiner asserted that the claimed method uses a composition that comprises hyperforin and that therefore, other ingredients are not excluded. Applicants have amended claim 46 to recite "consisting of" instead of "comprising." Valavichyus *et al.* teaches the use of extracts from St. John's wort and Chamomilla recutita in inhibiting tumor growth in rats. Claim 46 as amended precludes any ingredient except for hyperforin and the carrier in the treatment composition. This rejection is therefore obviated and applicants accordingly request that it be withdrawn.

Claim Rejection Under 35 U.S.C. §103

I. Paragraph 8 Of The Action

Claims 36 and 39-45 have been rejected under 35 U.S.C. §103 as being obvious in view of The Hypericum Home Page (1996) (the "HHP" hereafter). Applicants respectfully traverse this rejection.

First, applicants point out that the Examiner has not demonstrated that the relied upon disclosure was, in fact, available to the public as of the effective filing date of this application. Because the HHP is an Internet "home page" and such home pages are routinely up-dated and changed, there is no way to know from the face of this document whether the HHP printed out by the Examiner on 10/15/01 is the same home page that was publicly available in November 1998. It is the Examiner's burden to establish this proof and in the absence of such proof, the Examiner's rejection is improper and withdrawal thereof is respectfully requested.

However, in further response, applicants point out that the HHP lists components in St. John's wort extracts which include 0.06-0.75% hypericin and 2.8% hyperforin, among other things (pages 1 & 2). It provides the available pharmaceutical forms of Hypericum (St. John's wort), including tablets, capsules, drops, teas, as well as an oil for external use (page 2). For therapeutic and clinical applications, the HHP summarizes that Hypericum is effectively used for treatment of depression (pages 3 & 4). In its survey of a number of clinical studies, the HHP reports that anti-inflammatory and anti-bacterial effects of St. John's wort preparations have been observed with one study which were attributed to hyperforin (page 3). Further, the HHP mentions that hypericin has anticancer properties and can be used in cancer treatment.

The Examiner argues that, even though the HHP does not teach the effective amount of hyperforin and hypericin as claimed, it would have been obvious for a skilled artisan to experiment and come up with the effective amounts for treatment of various conditions as claimed. The Examiner further

argues that the HHP motivates a skilled artisan to embark on such experimentations.

Applicants submit that the kind of experimentation the Examiner envisions is far beyond a routine practice that necessitates foreseeable positive results. Based on the teaching of the HHP, a skilled artisan would know only that St. John's wort may be useful for treating cancer, inflammatory conditions, and bacterial infections. But applicants do not claim a method for treating the same using St. John's wort. Rather, applicants' claims are drawn to treatment methods for specific conditions using a composition consisting of a suitable carrier and (i) hyperforin or (ii) hyperforin and hypericin at effective amounts. The specification teaches the details of these effective amounts and treatment methods.

It is a qualitative--and hence nonobvious--leap from the general knowledge that St. John's wort may be useful for treating certain conditions to the specific treatment protocols of using hyperforin and hypericin at prescribed amounts. To cross such a chasm, a skilled artisan would have to (i) discover that it is hyperforin primarily--or hyperforin together with hypericin--that exert the desirable therapeutic effects for each of the conditions as claimed and (ii) discover effective amounts of hyperforin and/or hypericin for treating each of conditions as claimed. A mere HHP falls far short in equipping a skilled artisan for these discoveries. There is no suggestion or any reasonable expectation of success to make these discoveries, a situation similar to In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) where the Federal Circuit reverses the PTO's determination that applicants' claims are obvious (stating, in relevant part, that "[t]he prior art simply does not disclose or suggest the expression in cyanobacteria of a chimeric gene encoding an insecticidally active protein, or convey to those of ordinary skill a reasonable expectation of success in doing so.").

In fact, the elaborative details of the treatment protocols and the various compilations of effective amounts disclosed in the specification would manifest the undue burden of experimentation on a skilled artisan. There is simply no reasonable expectation of success for one of the ordinary skill to

arrive at applicants' invention based on the HHP. This prior art reference does not render obvious applicants' invention as claimed.

Accordingly, applicants request withdrawal of this rejection.

II. Paragraph 9 Of The Action

Claims 36-39 have been rejected under 35 U.S.C. §103 as being obvious and thus unpatentable over the HHP in view of The Merck Manual (the "MM" hereafter).

Essentially, the Examiner advanced the same arguments as that used to substantiate the rejection raised in paragraph 8 of the Action. In addition, the Examiner asserted that the MM provides that eczemas (including different types and variations) are characterized by inflammation and that, therefore, the HHP and MM together render obvious the methods of treating eczemas.

Applicants traverse this rejection for the same reasons as discussed in the previous section. First, the Examiner has not established that the relied upon disclosure in MM was, in fact, available to the public as of November, 1998. The Examiner must provide proof. Additionally, there is legitimate concern that the HHP is not prior art. The Examiner has not established that this is the case.

In any event, with regard to the merits of the rejection, applicants assert that the HHP, alone, cannot render obvious the claimed treatment methods for cancer, inflammation, or bacterial infection. The HHP, together with the MM, still fails to render obvious the claimed treatment methods for eczemas. There is no suggestion or reasonable expectation of success in the combined teachings of the HHP and MM for those of ordinary skill in the art to arrive at the effective amounts and treatment protocols for each claimed conditions. "Obvious to experiment" is not a proper standard for obviousness. See, e.g., Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 231 USPQ 81 (Fed. Cir., 1986); In re Dow Chemical Co. 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cirs. 1988).

Applicants respectfully request that this rejection be withdrawn.

III. Paragraph 10 Of The Action

Claims 46-49 have been rejected under 35 U.S.C. §103 as being obvious in view of Valavichyus *et al.*

Applicants traverse this rejection. Valavichyus *et al.* teaches the use of extracts from St. John's wort and Chamomilla recutita in inhibiting tumor growth in rats. There is no mention whatsoever in this reference what components in the mixed extracts contributed to the tumor inhibition effect. The Examiner asserted that, because these claims recite a composition comprising hyperforin, other ingredients are not excluded. Applicants have amended claim 46 to recite "consisting of" instead of "comprising" and claim 47 to recite "is" instead of "comprises." The claimed method as amended thus precludes any elements other than hyperforin and a suitable pharmaceutical carrier. Further, for the same reasons discussed in the previous two subsections, Valavichyus *et al.* fails to disclose or suggest the specific treatment protocols and effective amounts of hyperforin for various cancerous and precancerous conditions; and, further, it fails to provide any reasonable expectation of success for those of ordinary skill to arrive at these specific treatment protocols and effective amounts. Therefore, Valavichyus *et al.* cannot render obvious the claimed method of treatment.

Applicants accordingly request withdrawal of this rejection.

IV. Paragraph 11 Of The Action

Claims 46-54 have been rejected under 35 U.S.C. §103 as being obvious and thus unpatentable over Valavichyus *et al.* in view of the HHP and Decosterd *et al.*

Applicants respectfully traverse this rejection. The Examiner essentially argued the same points for this rejection as those for the rejection in paragraph 10 of the Action. In addition, the Examiner cited DeCosterd *et al.* which teaches that derivatives of hyperforin inhibit growth of colon

carcinomas. The Examiner stated: "[a]s evidenced by the cited references, at the time of the invention, hyperforin, derivatives thereof and extracts of Hypericum were well known as effective agents against cancers of various kinds." See, page 11, the Action.

Indeed, the general knowledge that hyperforin and derivatives and extracts of Hypericum may have anticancer effects is all that is taught by the cited references, alone, or in combination. As discussed in subsections I and III *supra*, applicants' invention goes far beyond the teachings of the cited art. The art does not disclose or suggest any specific protocols for treating tumors or effective amounts of hyperforin used in various cancerous or precancerous conditions, or provide any reasonable expectation of success for those skilled in the art to discover the same. Undue experimentation would be required.

Applicants have addressed the HTT and Valavichyus *et al.* in the previous subsections. As discussed in subsection III *supra*, Applicants have amended claim 46 to recite "consisting of" instead of "comprising" and claim 47 to recite "is" instead of "comprises," thereby precluding other elements in the treatment composition except for hyperforin and a suitable carrier. As for DeCosterd *et al.*, applicants submit that hyperforin derivatives are irrelevant to the obviousness determination of the claimed invention. Applicants only claim an effective amount of (i) hyperforin or (ii) hyperforin and hypericin in the treatment composition.

Accordingly, applicants request that this obviousness rejection be withdrawn.

In view of the forgoing amendments and remarks, applicants request that the amended claims be favorably considered.

CONCLUSION

In view of the above amendments and remarks, applicants believe the application is in condition for allowance and respectfully request entry of the amendments and notification of allowance.

Respectfully submitted,

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Date

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PDG/QS

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Please cancel claim 55. Please amend claims 40-49 and 56 to read as follows:

40. (Amended) The method according to claim 36, wherein said composition is in the form of a topical ointment and said effective amount consists of at least 15 μg hyperforin per ml **of the composition**.

41. (Amended) The method according to claim 36, wherein said composition is in the form of a topical ointment and said effective amount is 0.02-20 mg hyperforin per ml **of the composition**.

42. (Amended) The method according to claim 41 wherein said effective amount is 1-20 mg hyperforin per ml **of the composition**.

43. (Amended) The method according to claim 42. wherein said effective amount is 10 mg hyperforin per ml **of the composition**.

44 (Amended) The method according to claim 36, wherein said effective amount is at least 15 μg hypericin per ml **of the composition**.

45. (Amended) The method according to claim 36, wherein said effective amount of hypericin is 20-150 μg hypericin per ml **of the composition**.

46. (Amended) A method of treating cancer comprising administering to a subject in need thereof an effective amount of a composition [comprising]**consisting of** hyperforin and a pharmaceutically acceptable carrier.

47 (Amended) The method according to claim 46, wherein said effective amount [comprises]**is** at least 50 μg[/ml of] hyperforin **per ml of the composition** in a form suitable for injection into a tumor.

48. (Amended) The method according to claim 46, wherein said effective amount is at least 100 μg hyperforin per μl **of the composition** in a form suitable for epicutaneous application.

49. (Amended) The method according to claim 46, wherein said effective amount is at least 50 μg hyperforin per ml in plasma **post-administration** when administered systemically.

56. (Amended) The method of [one of]claim[s] 46[or 55], wherein said hyperforin is at least 90% pure.